

## SEQUENCE LISTING

<110> Mark J. Graham  
Andrew T. Watt

<120> ANTISENSE MODULATION OF COMPLEMENT COMPONENT C3 EXPRESSION

<130> RTS-0329

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&lt;220&gt;

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&lt;221&gt; CDS

&lt;222&gt; (61)...(5052)

&lt;400&gt; 3

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Met Gly Pro Thr Ser Gly Pro Ser Leu Leu Leu Leu Leu Thr His  
1 5 10 15ctc ccc ctg gct ctg ggg agt ccc atg tac tct atc atc acc ccc aac 156  
Leu Pro Leu Ala Leu Gly Ser Pro Met Tyr Ser Ile Ile Thr Pro Asn  
20 25 30atc ttg cgg ctg gag agc gag gag acc atg gtg ctg gag gcc cac gac 204  
Ile Leu Arg Leu Glu Ser Glu Glu Thr Met Val Leu Glu Ala His Asp  
35 40 45gcg caa ggg gat gtt cca gtc act gtt act gtc cac gac ttc cca ggc 252  
Ala Gln Gly Asp Val Pro Val Thr Val Thr Val His Asp Phe Pro Gly  
50 55 60aaa aaa cta gtg ctg tcc agt gag aag act gtg ctg acc cct gcc acc 300  
Lys Lys Leu Val Leu Ser Ser Glu Lys Thr Val Leu Thr Pro Ala Thr  
65 70 75 80aac cac atg ggc aac gtc acc ttc acg atc cca gcc aac agg gag ttc 348  
Asn His Met Gly Asn Val Thr Phe Thr Ile Pro Ala Asn Arg Glu Phe  
85 90 95aag tca gaa aag ggg cgc aac aag ttc gtg acc gtg cag gcc acc ttc 396  
Lys Ser Glu Lys Gly Arg Asn Lys Phe Val Thr Val Gln Ala Thr Phe  
100 105 110ggg acc caa gtg gtg gag aag gtg gtg ctg gtc agc ctg cag agc ggg 444  
Gly Thr Gln Val Val Glu Lys Val Val Leu Val Ser Leu Gln Ser Gly  
115 120 125

tac ctc ttc atc cag aca gac aag acc atc tac acc cct ggc tcc aca Tyr Leu Phe Ile Gln Thr Asp Lys Thr Ile Tyr Thr Pro Gly Ser Thr 130                   135                   140	492
gtt ctc tat cgg atc ttc acc gtc aac cac aag ctg cta ccc gtg ggc Val Leu Tyr Arg Ile Phe Thr Val Asn His Lys Leu Leu Pro Val Gly 145                   150                   155                   160	540
cgg acg gtc atg gtc aac att gag aac ccg gaa ggc atc ccg gtc aag Arg Thr Val Met Val Asn Ile Glu Asn Pro Glu Gly Ile Pro Val Lys 165                   170                   175	588
cag gac tcc ttg tct tct cag aac cag ctt ggc gtc ttg ccc ttg tct Gln Asp Ser Leu Ser Ser Gln Asn Gln Leu Gly Val Leu Pro Leu Ser 180                   185                   190	636
tgg gac att ccg gaa ctc gtc aac atg ggc cag tgg aag atc cga gcc Trp Asp Ile Pro Glu Leu Val Asn Met Gly Gln Trp Lys Ile Arg Ala 195                   200                   205	684
tac tat gaa aac tca cca cag cag gtc ttc tcc act gag ttt gag gtg Tyr Tyr Glu Asn Ser Pro Gln Gln Val Phe Ser Thr Glu Phe Glu Val 210                   215                   220	732
aag gag tac gtg ctg ccc agt ttc gag gtc ata gtg gag cct aca gag Lys Glu Tyr Val Leu Pro Ser Phe Glu Val Ile Val Glu Pro Thr Glu 225                   230                   235                   240	780
aaa ttc tac tac atc tat aac gag aag ggc ctg gag gtc acc atc acc Lys Phe Tyr Tyr Ile Tyr Asn Glu Lys Gly Leu Glu Val Thr Ile Thr 245                   250                   255	828
gcc agg ttc ctc tac ggg aag aaa gtg gag gga act gcc ttt gtc atc Ala Arg Phe Leu Tyr Gly Lys Lys Val Glu Gly Thr Ala Phe Val Ile 260                   265                   270	876
ttc ggg atc cag gat ggc gaa cag agg att tcc ctg cct gaa tcc ctc Phe Gly Ile Gln Asp Gly Glu Gln Arg Ile Ser Leu Pro Glu Ser Leu 275                   280                   285	924
aag cgc att ccg att gag gat ggc tcg ggg gag gtt gtg ctg agc cgg Lys Arg Ile Pro Ile Glu Asp Gly Ser Gly Glu Val Val Leu Ser Arg 290                   295                   300	972

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Lys Val Leu Leu Asp Gly Val Gln Asn Leu Arg Ala Glu Asp Leu Val  
305 310 315 320

ggg aag tct ttg tac gtg tct gcc acc gtc atc ttg cac tca ggc agt 1068  
Gly Lys Ser Leu Tyr Val Ser Ala Thr Val Ile Leu His Ser Gly Ser  
325 330 335

gac atg gtg cag gca gag cgc agc ggg atc ccc atc gtg acc tct ccc 1116  
Asp Met Val Gln Ala Glu Arg Ser Gly Ile Pro Ile Val Thr Ser Pro  
340 345 350

tac cag atc cac ttc acc aag aca ccc aag tac ttc aaa cca gga atg 1164  
Tyr Gln Ile His Phe Thr Lys Thr Pro Lys Tyr Phe Lys Pro Gly Met  
355 360 365

ccc ttt gac ctc atg gtg ttc gtg acg aac cct gat ggc tct cca gcc 1212  
Pro Phe Asp Leu Met Val Phe Val Thr Asn Pro Asp Gly Ser Pro Ala  
370 375 380

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Tyr Arg Val Pro Val Ala Val Gln Gly Glu Asp Thr Val Gln Ser Leu  
385 390 395 400

acc cag gga gat ggc gtg gcc aaa ctc agc atc aac aca cac ccc agc 1308  
Thr Gln Gly Asp Gly Val Ala Lys Leu Ser Ile Asn Thr His Pro Ser  
405 410 415

cag aag ccc ttg agc atc acg gtg cgc acg aag aag cag gag ctc tcg 1356  
Gln Lys Pro Leu Ser Ile Thr Val Arg Thr Lys Lys Gln Glu Leu Ser  
420 425 430

gag gca gag cag gct acc agg acc atg cag gct ctg ccc tac agc acc 1404  
Glu Ala Glu Gln Ala Thr Arg Thr Met Gln Ala Leu Pro Tyr Ser Thr  
435 440 445

gtg ggc aac tcc aac aat tac ctg cat ctc tca gtg cta cgt aca gag 1452  
Val Gly Asn Ser Asn Asn Tyr Leu His Leu Ser Val Leu Arg Thr Glu  
450 455 460

ctc aga ccc ggg gag acc ctc aac gtc aac ttc ctc ctg cga atg gac 1500  
Leu Arg Pro Gly Glu Thr Leu Asn Val Asn Phe Leu Leu Arg Met Asp  
465 470 475 480

cgc gcc cac gag gcc aag atc cgc tac tac acc tac ctg atc atg aac 1548  
Arg Ala His Glu Ala Lys Ile Arg Tyr Tyr Thr Tyr Leu Ile Met Asn  
485 490 495

aag ggc agg ctg ttg aag gcg gga cgc cag gtg cga gag ccc ggc cag 1596  
Lys Gly Arg Leu Leu Lys Ala Gly Arg Gln Val Arg Glu Pro Gly Gln  
500 505 510

gac ctg gtg gtg ctg ccc ctg tcc atc acc acc gac ttc atc cct tcc 1644  
Asp Leu Val Val Leu Pro Leu Ser Ile Thr Thr Asp Phe Ile Pro Ser  
515 520 525

ttc cgc ctg gtg gcg tac tac acg ctg atc ggt gcc agc ggc cag agg 1692  
Phe Arg Leu Val Ala Tyr Tyr Thr Leu Ile Gly Ala Ser Gly Gln Arg  
530 535 540

gag gtg gtg gcc gac tcc gtg tgg gtg gac gtc aag gac tcc tgc gtg 1740  
Glu Val Val Ala Asp Ser Val Trp Val Asp Val Lys Asp Ser Cys Val  
545 550 555 560

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Gly Ser Leu Val Val Lys Ser Gly Gln Ser Glu Asp Arg Gln Pro Val  
565 570 575

cct ggg cag cag atg acc ctg aag ata gag ggt gac cac ggg gcc cgg 1836  
Pro Gly Gln Gln Met Thr Leu Lys Ile Glu Gly Asp His Gly Ala Arg  
580 585 590

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Val Val Leu Val Ala Val Asp Lys Gly Val Phe Val Leu Asn Lys Lys  
595 600 605

aac aaa ctg acg cag agt aag atc tgg gac gtg gtg gag aag gca gac 1932  
Asn Lys Leu Thr Gln Ser Lys Ile Trp Asp Val Val Glu Lys Ala Asp  
610 615 620

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Ile Gly Cys Thr Pro Gly Ser Gly Lys Asp Tyr Ala Gly Val Phe Ser  
625 630 635 640

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645 650 655

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Arg Ala Glu Leu Gln Cys Pro Gln Pro Ala Ala Arg Arg Arg Arg Ser			
660	665	670	
gtg cag ctc acg gag aag cga atg gac aaa gtc ggc aag tac ccc aag			2124
Val Gln Leu Thr Glu Lys Arg Met Asp Lys Val Gly Lys Tyr Pro Lys			
675	680	685	
gag ctg cgc aag tgc tgc gag gac ggc atg cgg gag aac ccc atg agg			2172
Glu Leu Arg Lys Cys Cys Glu Asp Gly Met Arg Glu Asn Pro Met Arg			
690	695	700	
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Phe Ser Cys Gln Arg Arg Thr Arg Phe Ile Ser Leu Gly Glu Ala Cys			
705	710	715	720
aag aag gtc ttc ctg gac tgc aac tac atc aca gag ctg cgg cgg			2268
Lys Lys Val Phe Leu Asp Cys Cys Asn Tyr Ile Thr Glu Leu Arg Arg			
725	730	735	
cag cac gcg cgg gcc agc cac ctg ggc ctg gcc agg agt aac ctg gat			2316
Gln His Ala Arg Ala Ser His Leu Gly Leu Ala Arg Ser Asn Leu Asp			
740	745	750	
gag gac atc att gca gaa gag aac atc gtt tcc cga agt gag ttc cca			2364
Glu Asp Ile Ile Ala Glu Glu Asn Ile Val Ser Arg Ser Glu Phe Pro			
755	760	765	
gag agc tgg ctg tgg aac gtt gag gac ttg aaa gag cca ccg aaa aat			2412
Glu Ser Trp Leu Trp Asn Val Glu Asp Leu Lys Glu Pro Pro Lys Asn			
770	775	780	
gga atc tct acg aag ctc atg aat ata ttt ttg aaa gac tcc atc acc			2460
Gly Ile Ser Thr Lys Leu Met Asn Ile Phe Leu Lys Asp Ser Ile Thr			
785	790	795	800
acg tgg gag att ctg gct gtc agc atg tcg gac aag aaa ggg atc tgt			2508
Thr Trp Glu Ile Leu Ala Val Ser Met Ser Asp Lys Lys Gly Ile Cys			
805	810	815	
gtg gca gac ccc ttc gag gtc aca gta atg cag gac ttc ttc atc gac			2556
Val Ala Asp Pro Phe Glu Val Thr Val Met Gln Asp Phe Phe Ile Asp			
820	825	830	

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Leu Arg Leu Pro Tyr Ser Val Val Arg Asn Glu Gln Val Glu Ile Arg  
835 840 845

gcc gtt ctc tac aat tac cgg cag aac caa gag ctc aag gtg agg gtg 2652  
Ala Val Leu Tyr Asn Tyr Arg Gln Asn Gln Glu Leu Lys Val Arg Val  
850 855 860

gaa cta ctc cac aat cca gcc ttc tgc agc ctg gcc acc acc aag agg 2700  
Glu Leu Leu His Asn Pro Ala Phe Cys Ser Leu Ala Thr Thr Lys Arg  
865 870 875 880

cgt cac cag cag acc gta acc atc ccc ccc aag tcc tcg ttg tcc gtt 2748  
Arg His Gln Gln Thr Val Thr Ile Pro Pro Lys Ser Ser Leu Ser Val  
885 890 895

cca tat gtc atc gtg ccg cta aag acc ggc ctg cag gaa gtg gaa gtc 2796  
Pro Tyr Val Ile Val Pro Leu Lys Thr Gly Leu Gln Glu Val Glu Val  
900 905 910

aag gct gcc gtc tac cat cat ttc atc agt gac ggt gtc agg aag tcc 2844  
Lys Ala Ala Val Tyr His His Phe Ile Ser Asp Gly Val Arg Lys Ser  
915 920 925

ctg aag gtc gtg ccg gaa gga atc aga atg aac aaa act gtg gct gtt 2892  
Leu Lys Val Val Pro Glu Gly Ile Arg Met Asn Lys Thr Val Ala Val  
930 935 940

cgc acc ctg gat cca gaa cgc ctg ggc cgt gaa gga gtg cag aaa gag 2940  
Arg Thr Leu Asp Pro Glu Arg Leu Gly Arg Glu Gly Val Gln Lys Glu  
945 950 955 960

gac atc cca cct gca gac ctc agt gac caa gtc ccg gac acc gag tct 2988  
Asp Ile Pro Pro Ala Asp Leu Ser Asp Gln Val Pro Asp Thr Glu Ser  
965 970 975

gag acc aga att ctc ctg caa ggg acc cca gtg gcc cag atg aca gag 3036  
Glu Thr Arg Ile Leu Leu Gln Gly Thr Pro Val Ala Gln Met Thr Glu  
980 985 990

gat gcc gtc gac gcg gaa cgg ctg aag cac ctc att gtg acc ccc tcg 3084  
Asp Ala Val Asp Ala Glu Arg Leu Lys His Leu Ile Val Thr Pro Ser  
995 1000 1005

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Gly Cys Gly Glu Gln Asn Met Ile Gly Met Thr Pro Thr Val Ile Ala  
1010 1015 1020

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Val His Tyr Leu Asp Glu Thr Glu Gln Trp Glu Lys Phe Gly Leu Glu  
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aag cgg cag ggg gcc ttg gag ctc atc aag aag ggg tac acc cag cag 3228  
Lys Arg Gln Gly Ala Leu Glu Leu Ile Lys Lys Gly Tyr Thr Gln Gln  
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gca ccc agc acc tgg ctg acc gcc tac gtg gtc aag gtc ttc tct ctg 3324  
Ala Pro Ser Thr Trp Leu Thr Ala Tyr Val Val Lys Val Phe Ser Leu  
1075 1080 1085

gct gtc aac ctc atc gcc atc gac tcc caa gtc ctc tgc ggg gct gtt 3372  
Ala Val Asn Leu Ile Ala Ile Asp Ser Gln Val Leu Cys Gly Ala Val  
1090 1095 1100

aaa tgg ctg atc ctg gag aag cag aag ccc gac ggg gtc ttc cag gag 3420  
Lys Trp Leu Ile Leu Glu Lys Gln Lys Pro Asp Gly Val Phe Gln Glu  
1105 1110 1115 1120

gat gcg ccc gtg ata cac caa gaa atg att ggt gga tta cgg aac aac 3468  
Asp Ala Pro Val Ile His Gln Glu Met Ile Gly Gly Leu Arg Asn Asn  
1125 1130 1135

aac gag aaa gac atg gcc ctc acg gcc ttt gtt ctc atc tcg ctg cag 3516  
Asn Glu Lys Asp Met Ala Leu Thr Ala Phe Val Leu Ile Ser Leu Gln  
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gag gct aaa gat att tgc gag gag cag gtc aac agc ctg cca ggc agc 3564  
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Ile Thr Lys Ala Gly Asp Phe Leu Glu Ala Asn Tyr Met Asn Leu Gln  
1170 1175 1180

aga tcc tac act gtg gcc att gct ggc tat gct ctg gcc cag atg ggc 3660  
Arg Ser Tyr Thr Val Ala Ile Ala Gly Tyr Ala Leu Ala Gln Met Gly  
1185 1190 1195 1200

agg ctg aag ggg cct ctt aac aaa ttt ctg acc aca gcc aaa gat 3708  
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Gly Tyr Gly Ser Thr Gln Ala Thr Phe Met Val Phe Gln Ala Leu Ala  
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Ser Leu Gln Leu Pro Ser Arg Ser Ser Lys Ile Thr His Arg Ile His  
1300 1305 1310

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Trp Glu Ser Ala Ser Leu Leu Arg Ser Glu Glu Thr Lys Glu Asn Glu  
1315 1320 1325

ggt ttc aca gtc aca gct gaa gga aaa ggc caa ggc acc ttg tcg gtg 4092  
Gly Phe Thr Val Thr Ala Glu Gly Lys Gly Gln Gly Thr Leu Ser Val  
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gtg aca atg tac cat gct aag gcc aaa gat caa ctc acc tgt aat aaa 4140  
Val Thr Met Tyr His Ala Lys Ala Lys Asp Gln Leu Thr Cys Asn Lys  
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ttc gac ctc aag gtc acc ata aaa cca gca ccg gaa aca gaa aag agg 4188  
Phe Asp Leu Lys Val Thr Ile Lys Pro Ala Pro Glu Thr Glu Lys Arg  
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Pro Gln Asp Ala Lys Asn Thr Met Ile Leu Glu Ile Cys Thr Arg Tyr  
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1395 1400 1405

act ggc ttt gct cca gac aca gat gac ctg aag cag ctg gcc aat ggt 4332  
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Asp Cys Leu Ala Phe Lys Val His Gln Tyr Phe Asn Val Glu Leu Ile  
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cag cct gga gca gtc aag gtc tac gcc tat tac aac ctg gag gaa agc 4524  
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1490 1495 1500

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Cys Glu Pro Gly Val Asp Tyr Val Tyr Lys Thr Arg Leu Val Lys Val		
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Ile Ser Pro Ile Lys Cys Arg Glu Ala Leu Lys Leu Glu Glu Lys Lys		
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His Tyr Leu Met Trp Gly Leu Ser Ser Asp Phe Trp Gly Glu Lys Pro		
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Asn Leu Ser Tyr Ile Ile Gly Lys Asp Thr Trp Val Glu His Trp Pro		
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gag gag gac gaa tgc caa gac gaa gag aac cag aaa caa tgc cag gac		5004
Glu Glu Asp Glu Cys Gln Asp Glu Glu Asn Gln Lys Gln Cys Gln Asp		
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ctc ggc gcc ttc acc gag agc atg gtt gtc ttt ggg tgc ccc aac tga		5052
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&lt;223&gt; PCR Primer

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cctgcccctt accccttcat tccttccacc tttttcccttc actatgggac cagcttcagg 180

gtccccagcta ctatgtctac tgctgctgtt ggccagctcc ccattagctc tggggatccc 240

catgttaagta gttacctttt ggggggtgcag tttcttatac aattnaggag tcacctaggt 300

gagtcaccta ggagtcaccc acttgggggg agacagggat gtaagaatt tgtgctgggg 360  
gctggaggat ggctcagtgg gtatgaagtc ttgctgcatt gacataagga ccttaactca 420  
aactcccagc acccacagaa aagccaggag tggcctccag agcctgtAAC cccacactgt 480  
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agatgttGAC tcaaggTGTG gggaggGAGG ggcataGAAC aggacaccGG acatTTcCT 600  
gtgacgtgac atacatacat acatacatac atacatacat acatacatac aaacagagag 660  
aaagagagag aatgtgagtg tttgggttgt ctatgttca tagaactcag gtattgtAGC 720  
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&lt;210&gt; 54

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&lt;213&gt; Artificial Sequence

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&lt;211&gt; 20

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&lt;213&gt; Artificial Sequence

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Gly Pro Ala Ser Gly Ser Gln Leu Leu Val Leu Leu Leu Leu Ala  
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Ser Ser Pro Leu Ala Leu Gly Ile Pro Met Tyr Ser Ile Ile Thr Pro  
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Asn Val Leu Arg Leu Glu Ser Glu Glu Thr Ile Val Leu Glu Ala His  
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Asp Ala Gln Gly Asp Ile Pro Val Thr Val Thr Val Gln Asp Phe Leu  
50 55 60 65

aag agg caa gtg ctg acc agt gag aag aca gtg ttg aca gga gcc agt 299  
Lys Arg Gln Val Leu Thr Ser Glu Lys Thr Val Leu Thr Gly Ala Ser  
70 75 80

gga cat ctg aga agc gtc tcc atc aag att cca gcc agt aag gaa ttc 347  
Gly His Leu Arg Ser Val Ser Ile Lys Ile Pro Ala Ser Lys Glu Phe  
85 90 95

aac tca gat aag gag ggg cac aag tac gtg aca gtg gtg gca aac ttc 395  
Asn Ser Asp Lys Glu Gly His Lys Tyr Val Thr Val Val Ala Asn Phe  
100 105 110

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Gly Glu Thr Val Val Glu Lys Ala Val Met Val Ser Phe Gln Ser Gly  
115 120 125

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Tyr Leu Phe Ile Gln Thr Asp Lys Thr Ile Tyr Thr Pro Gly Ser Thr  
130 135 140 145

gtc tta tat cgg atc ttc act gtg gac aac aac cta ctg ccc gtg ggc 539  
Val Leu Tyr Arg Ile Phe Thr Val Asp Asn Asn Leu Leu Pro Val Gly  
150 155 160

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Lys Thr Val Val Ile Leu Ile Glu Thr Pro Asp Gly Ile Pro Val Lys  
165 170 175

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Arg Asp Ile Leu Ser Ser Asn Asn Gln His Gly Ile Leu Pro Leu Ser  
180 185 190

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Trp Asn Ile Pro Glu Leu Val Asn Met Gly Gln Trp Lys Ile Arg Ala  
195 200 205

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Phe Tyr Glu His Ala Pro Lys Gln Ile Phe Ser Ala Glu Phe Glu Val  
210 215 220 225

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Lys Glu Tyr Val Leu Pro Ser Phe Glu Val Arg Val Glu Pro Thr Glu  
230 235 240

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Thr Phe Tyr Tyr Ile Asp Asp Pro Asn Gly Leu Glu Val Ser Ile Ile  
245 250 255

gcc aag ttc ctg tac ggg aaa aac gtg gac ggg aca gcc ttc gtg att 875  
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260 265 270

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Phe Gly Val Gln Asp Gly Asp Lys Lys Ile Ser Leu Ala His Ser Leu  
275 280 285

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Thr Arg Val Val Ile Glu Asp Gly Val Gly Asp Ala Val Leu Thr Arg  
290 295 300 305

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310 315 320

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Gly Lys Ser Leu Tyr Val Ser Val Thr Val Ile Leu His Ser Gly Ser  
325 330 335

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340 345 350

tac cag atc cac ttc acc aag aca ccc aaa ttc ttc aag cca gcc atg 1163

Tyr Gln Ile His Phe Thr Lys Thr Pro Lys Phe Phe Lys Pro Ala Met  
355 360 365

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Pro Phe Asp Leu Met Val Phe Val Thr Asn Pro Asp Gly Ser Pro Ala  
370 375 380 385

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390 395 400

caa gat gat ggc gtg gcc aag cta agc atc aac aca ccc aac agc cgc 1307  
Gln Asp Asp Gly Val Ala Lys Leu Ser Ile Asn Thr Pro Asn Ser Arg  
405 410 415

caa ccc ctg acc atc aca gtc cgc acc aag aag gac act ctc cca gaa 1355  
Gln Pro Leu Thr Ile Thr Val Arg Thr Lys Lys Asp Thr Leu Pro Glu  
420 425 430

tca cgg cag gcc acc aag aca atg gag gcc cat ccc tac agc act atg 1403  
Ser Arg Gln Ala Thr Lys Thr Met Glu Ala His Pro Tyr Ser Thr Met  
435 440 445

cac aac tcc aac aac tac cta cac ttg tca gtg tca cga atg gag ctc 1451  
His Asn Ser Asn Asn Tyr Leu His Leu Ser Val Ser Arg Met Glu Leu  
450 455 460 465

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Lys Pro Gly Asp Asn Leu Asn Val Asn Phe His Leu Arg Thr Asp Pro  
470 475 480

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Gly His Glu Ala Lys Ile Arg Tyr Tyr Tyr Leu Val Met Asn Lys  
485 490 495

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Gly Lys Leu Leu Lys Ala Gly Arg Gln Val Arg Glu Pro Gly Gln Asp  
500 505 510

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Leu Val Val Leu Ser Leu Pro Ile Thr Pro Glu Phe Ile Pro Ser Phe  
515 520 525

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Arg Leu Val Ala Tyr Tyr Thr Leu Ile Gly Ala Ser Gly Gln Arg Glu  
530 535 540 545

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Val Val Ala Asp Ser Val Trp Val Asp Val Lys Asp Ser Cys Ile Gly  
550 555 560

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Thr Leu Val Val Lys Gly Asp Pro Arg Asp Asn His Leu Ala Pro Gly  
565 570 575

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580 585 590

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595 600 605

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610 615 620 625

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Cys Thr Pro Gly Ser Gly Lys Asn Tyr Ala Gly Val Phe Met Asp Ala  
630 635 640

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645 650 655

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660 665 670

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675 680 685

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690 695 700 705

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Ser Cys Gln Arg Arg Ala Arg Leu Ile Thr Gln Gly Glu Asn Cys Ile  
710 715 720

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Lys Ala Phe Ile Asp Cys Cys Asn His Ile Thr Lys Leu Arg Glu Gln  
725 730 735

cac aga aga gac cac gtg ctg ggc ctg gcc agg agt gaa ttg gag gaa 2315  
His Arg Arg Asp His Val Leu Gly Leu Ala Arg Ser Glu Leu Glu Glu  
740 745 750

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755 760 765

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Ser Trp Leu Trp Thr Ile Glu Glu Leu Lys Glu Pro Glu Lys Asn Gly  
770 775 780 785

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790 795 800

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805 810 815

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835 840 845

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885 890 895

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Ala Val Asp Gly Glu Arg Leu Lys His Leu Ile Val Thr Pro Ala Gly  
995 1000 1005

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Cys Gly Glu Gln Asn Met Ile Gly Met Thr Pro Thr Val Ile Ala Val  
1010 1015 1020 1025

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Arg Gln Glu Ala Leu Glu Leu Ile Lys Lys Gly Tyr Thr Gln Gln Leu  
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Ala Phe Lys Gln Pro Ser Ser Ala Tyr Ala Ala Phe Asn Asn Arg Pro  
1060 1065 1070

ccc agc acc tgg ctg aca gcc tac gtg gtc aag gtc ttc tct cta gct 3323  
Pro Ser Thr Trp Leu Thr Ala Tyr Val Val Lys Val Phe Ser Leu Ala  
1075 1080 1085

gcc aac ctc atc gcc atc gac tct cac gtc ctg tgt ggg gct gtt aaa 3371  
Ala Asn Leu Ile Ala Ile Asp Ser His Val Leu Cys Gly Ala Val Lys  
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1110 1115 1120

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Gly Pro Val Ile His Gln Glu Met Ile Gly Gly Phe Arg Asn Ala Lys  
1125 1130 1135

gag gca gat gtg tca ctc aca gcc ttc gtc ctc atc gca ctg cag gaa 3515  
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1140 1145 1150

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1155 1160 1165

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1170 1175 1180 1185

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Pro Tyr Thr Val Ala Ile Ala Gly Tyr Ala Leu Ala Leu Met Asn Lys  
1190 1195 1200

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1205 1210 1215

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Ser Tyr Ala Leu Leu Ala Leu Leu Leu Lys Asp Phe Asp Ser Val  
1235 1240 1245

ccc cct gta gtg cgc tgg ctc aat gag caa aga tac tac gga ggc ggc 3851  
Pro Pro Val Val Arg Trp Leu Asn Glu Gln Arg Tyr Tyr Gly Gly  
1250 1255 1260 1265

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1270 1275 1280

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Tyr Gln Thr Asp Val Pro Asp His Lys Asp Leu Asn Met Asp Val Ser  
1285 1290 1295

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1300 1305 1310

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Phe Ser Leu Thr Ala Lys Gly Lys Gly Arg Gly Thr Leu Ser Val Val  
1330 1335 1340 1345

gca gtg tat cat gcc aaa ctc aaa agc aaa gtc acc tgc aag aag ttt 4139  
Ala Val Tyr His Ala Lys Leu Lys Ser Lys Val Thr Cys Lys Lys Phe  
1350 1355 1360

gac ctc agg gtc agc ata aga cca gcc cct gag aca gcc aag aag ccc 4187  
Asp Leu Arg Val Ser Ile Arg Pro Ala Pro Glu Thr Ala Lys Lys Pro  
1365 1370 1375

gag gaa gcc aag aat acc atg ttc ctt gaa atc tgc acc aag tac ttg 4235  
Glu Glu Ala Lys Asn Thr Met Phe Leu Glu Ile Cys Thr Lys Tyr Leu  
1380 1385 1390

gga gat gtg gac gcc act atg tcc atc ctg gac atc tcc atg atg act 4283  
Gly Asp Val Asp Ala Thr Met Ser Ile Leu Asp Ile Ser Met Met Thr  
1395 1400 1405

ggc ttt gct cca gac aca aag gac ctg gaa ctg ctg gcc tct gga gta 4331

Gly Phe Ala Pro Asp Thr Lys Asp Leu Glu Leu Leu Ala Ser Gly Val  
 1410                    1415                    1420                    1425                    4379  
 gat aga tac atc tcc aag tac gag atg aac aaa gcc ttc tcc aac aag  
 Asp Arg Tyr Ile Ser Lys Tyr Glu Met Asn Lys Ala Phe Ser Asn Lys  
 1430                    1435                    1440  
 aac acc ctc atc atc tac cta gaa aag att tca cac acc gaa gaa gac                    4427  
 Asn Thr Leu Ile Ile Tyr Leu Glu Lys Ile Ser His Thr Glu Glu Asp  
 1445                    1450                    1455  
 tgc ctg acc ttc aaa gtt cac cag tac ttt aat gtg gga ctt atc cag                    4475  
 Cys Leu Thr Phe Lys Val His Gln Tyr Phe Asn Val Gly Leu Ile Gln  
 1460                    1465                    1470  
 ccc ggg tcg gtc aag gtc tac tcc tat tac aac ctc gag gaa tca tgc                    4523  
 Pro Gly Ser Val Lys Val Tyr Ser Tyr Tyr Asn Leu Glu Glu Ser Cys  
 1475                    1480                    1485  
 acc cgg ttc tat cat cca gag aag gac gat ggg atg ctc agc aag ctg                    4571  
 Thr Arg Phe Tyr His Pro Glu Lys Asp Asp Gly Met Leu Ser Lys Leu  
 1490                    1495                    1500                    1505  
 tgc cac agt gaa atg tgc cgg tgt gct gaa gag aac tgc ttc atg caa                    4619  
 Cys His Ser Glu Met Cys Arg Cys Ala Glu Glu Asn Cys Phe Met Gln  
 1510                    1515                    1520  
 cag tca cag gag aag atc aac ctg aat gtc cgg cta gac aag gct tgt                    4667  
 Gln Ser Gln Glu Lys Ile Asn Leu Asn Val Arg Leu Asp Lys Ala Cys  
 1525                    1530                    1535  
 gag ccc gga gtc gac tat gtg tac aag acc gag cta acc aac ata aag                    4715  
 Glu Pro Gly Val Asp Tyr Val Tyr Lys Thr Glu Leu Thr Asn Ile Lys  
 1540                    1545                    1550  
 ctg ttg gat gat ttt gat gag tac acc atg acc atc cag cag gtc atc                    4763  
 Leu Leu Asp Asp Phe Asp Glu Tyr Thr Met Thr Ile Gln Gln Val Ile  
 1555                    1560                    1565  
 aag tca ggc tca gat gag gtg cag gca ggg cag caa cgc aag ttc atc                    4811  
 Lys Ser Gly Ser Asp Glu Val Gln Ala Gly Gln Gln Arg Lys Phe Ile  
 1570                    1575                    1580                    1585  
 agc cac atc aag tgc aga aac gcc ctg aag ctg cag aaa ggg aag aag                    4859

Ser His Ile Lys Cys Arg Asn Ala Leu Lys Leu Gln Lys Gly Lys Lys  
1590 1595 1600 4907  
tac ctc atg tgg ggc ctc tcc tct gac ctc tgg gga gaa aag ccc aac  
Tyr Leu Met Trp Gly Leu Ser Ser Asp Leu Trp Gly Glu Lys Pro Asn  
1605 1610 1615  
acc agc tac atc att ggg aag gac acg tgg gtg gag cac tgg cct gag 4955  
Thr Ser Tyr Ile Ile Gly Lys Asp Thr Trp Val Glu His Trp Pro Glu  
1620 1625 1630  
gca gaa gaa tgc cag gat cag aag tac cag aaa cag tgc gaa gaa ctt 5003  
Ala Glu Glu Cys Gln Asp Gln Lys Tyr Gln Lys Gln Cys Glu Glu Leu  
1635 1640 1645  
ggg gca ttc aca gaa tct atg gtg gtt tat ggt tgt ccc aac tga 5048  
Gly Ala Phe Thr Glu Ser Met Val Val Tyr Gly Cys Pro Asn  
1650 1655 1660  
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<220>

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ttccccacca gtgggtgtct ggccctctctc tgtcaaggct gcagggactg aatgagcctt 180  
agagtccctt aagcaccagc tttatgcggc tttgaaattha aaaatccata actgagggt 240  
ctgcaccagg ccctctctgg tcattggtgg gtgaagatgt caatctatct actaaaacca 300  
atcgagtcctc agctgggttt cctataactc cgccccagct gacagcctac gtggtcaagg 360  
tcttctctct agctgccaac ctcatgcaca tcgactctca cgtccctgtgt ggggctgtta 420

aatggttgat tctggagaaa cagaagccgg atggtgtctt tcaggaggat gggcccgta 480

ttcaccaaga aatg 494

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<220>

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<400> 114

cagcagtagc actagtagct 20

<210> 115

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<210> 117  
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<210> 123  
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<210> 126

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<210> 137

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<210> 139

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<212> DNA

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<210> 140  
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&lt;223&gt; Antisense Oligonucleotide

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<210> 141  
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&lt;223&gt; Antisense Oligonucleotide

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<210> 142  
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&lt;220&gt;

&lt;223&gt; Antisense Oligonucleotide

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&lt;210&gt; 150

&lt;211&gt; 20

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Antisense Oligonucleotide

&lt;400&gt; 150

ttcctgcagt gcgatgagga

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&lt;210&gt; 151

&lt;211&gt; 20

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Antisense Oligonucleotide

&lt;400&gt; 151

ttgacctgcc cctcacagat

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&lt;210&gt; 152

&lt;211&gt; 20

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Antisense Oligonucleotide

&lt;400&gt; 152

cctgccttgt tgatgctccc

20

&lt;210&gt; 153

&lt;211&gt; 20

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<400> 153

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<210> 154

<211> 20

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<213> Artificial Sequence

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<400> 159

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<210> 162  
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<400> 163

tgaccctgag gtcaaaacttc

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<210> 164

<211> 20

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<210> 165

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<213> Artificial Sequence

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<223> Antisense Oligonucleotide

<400> 165

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<210> 166

<211> 20

<212> DNA

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<220>

<223> Antisense Oligonucleotide

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<210> 167  
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&lt;220&gt;

&lt;223&gt; Antisense Oligonucleotide

<400> 167  
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<210> 168  
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&lt;220&gt;

&lt;223&gt; Antisense Oligonucleotide

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<210> 169  
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&lt;220&gt;

&lt;223&gt; Antisense Oligonucleotide

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&lt;210&gt; 170

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<400> 173

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<210> 174

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<210> 175

<211> 20

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<223> Antisense Oligonucleotide

<400> 175

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<210> 176

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<400> 176

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<210> 177  
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<400> 177  
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<210> 178  
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<210> 179  
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<400> 179  
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20